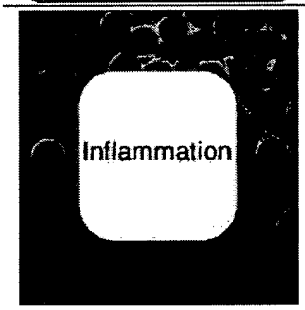

Inflammation

Introduction
Under normal circumstances, inflammation is an important defensive response to injury and infectio process begins with the recruitment of white blood cells, or leukocytes, from the circulatory system i of damaged or infected tissue. But excessive or prolonged accumulation of leukocytes can lead to **inflammatory** conditions, including rheumatoid arthritis, **inflammatory** bowel disease, psoriasis, m sclerosis, asthma and **septic shock**.

Antibodies and soluble receptors have been developed that neutralize the activities of particular **inflammatory** messengers. Enbrel™, a soluble **inflammatory** messenger receptor, has validated th for the treatment of rheumatoid arthritis. We believe that an orally available drug of comparable effi would represent a competitive advantage over drugs that must be injected, such as Enbrel™. The po market opportunity is enormous for drugs that would treat **inflammatory** conditions such as **inflam** bowel disease, psoriais, multiple sclerosis, and other **inflammatory** conditions more effectively thar treatments. About one American in five suffers from one of these diseases.

Program Status
Inflammatory messengers act by binding to specific cell-surface receptors that, in turn, set off sigr events culminating in the expression of many **inflammatory** response genes. Several key **inflamm** response genes are regulated by a single transcription factor, NF-κB. Our scientists have discovered novel regulatory proteins in the gene regulation pathways leading from the receptors for particular **inflammatory** messengers and have elucidated their roles in NF-κB activation. On the basis of thes discoveries, our scientists are recognized as leaders in this field of research.

Some of the regulatory proteins we have discovered represent ideal drug targets. We are engaged ir clinical development of a series of compounds that inhibit one of the key components involved in NF activation and have demonstrated oral activity in animal models of inflammation. We believe that ou discoveries and the expertise we have developed in this disease area place us in a leading position t the next generation of important anti-**inflammatory** drugs.

Septic Shock

Alternate Names : Bacteremic **Shock**, Endotoxic **Shock**, Septicemic **Shock**, Warm **Shock**

ADAM.

Definition

Septic shock is a serious, abnormal condition that occurs when an overwhelming infection leads to low blood pressure and low blood flow. Vital organs, such as the brain, heart, kidneys, and liver may not function properly or may fail. Decreased urine output from kidney failure may be one manifestation.

Overview, Causes, & Risk Factors

Septic shock occurs most often in the very old and the very young. It also occurs in people with underlying illnesses. Any bacterial organism can cause **septic shock**. Fungi and (rarely) viruses may also cause this condition. Toxins released by the bacteria or fungus may cause direct tissue damage, and may lead to low blood pressure and/or poor organ function.

These toxins also produce a vigorous inflammatory response from the body which contributes to **septic shock**.

Risk factors include underlying illnesses, such as diabetes; hematologic cancers (lymphoma or leukemia); and other malignancies and diseases of the genitourinary system, liver or biliary system, and intestinal system. Other risk factors are recent infection, prolonged antibiotic therapy, and having had a recent surgical or medical procedure. See also:

- Meningococcemia
- Waterhouse-Friderichsen syndrome
- DIC (disseminated intravascular coagulation)
- Multiple organ dysfunction syndrome (MODS)
- ARDS

Featu

- GER
- Hea
- Schi

- Aller
- Arth
- Asth
- Back
- Depi
- Diab
- Ecze

Derma

- Geni
- Hair
- Stre

Manac

< **Previous** ^ Top **Next** >

Jump to another section

- **Definition**
- **Septic Shock Overview, Causes, & Risk Factors**
- **Septic Shock** Symptoms & Signs

- **Septic Shock** Prevention
- **Septic Shock** Diagnosis & Tests
- **Septic Shock** Treatment
- **Septic Shock** Prognosis
- **Septic Shock** Complications
- Calling Your Health Care Provider

Topics that might be of interest to you

Diseases & Conditions

- Diabetes
- DIC (Disseminated Intravascular Coagulation)
- Heart Failure
- Meningococcemia
- Waterhouse-Friderichsen Syndrome

Tests & Exams

- Blood Culture

Other Topics

- Agitation
- Biliary System
- Blood Pressure - Low
- Confusion
- Fever
- Intravenous
- Paleness
- Respiratory
- **Shock**
- Toxins
- Urine Output - Decreased

Review Date : 1/25/2002
Reviewed By : David A. Kaufman, M.D., Pulmonary & Critical Care Medicine, University of Pennsylvania Medical Center, Philadelphia, PA. Review provided by VeriMed Healthcare Network.

Main Page of **Septic Shock**

Health Topics: A-Al Am-Az B C-Cj Ck-Cz D E F G H I J K L M N O P-Pl Pm-Pz Q R S-Sl Sm-Sz T U V W X Y Z 0-9

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[General]

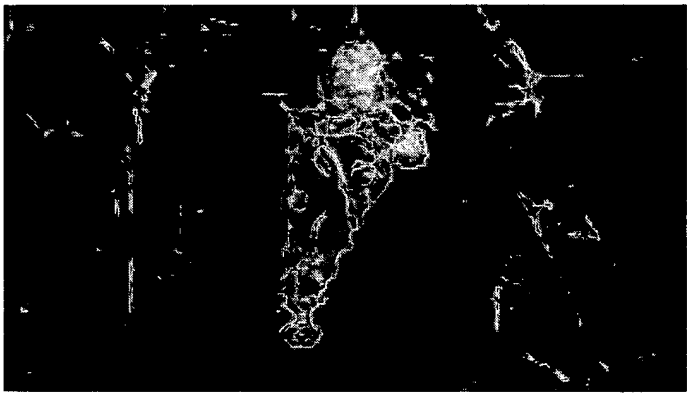
(See also Neonatal Sepsis and Neonatal Meningitis under Neonatal Infections in Ch. 260.)

Bacteremia and **septic shock** are closely related conditions. **Bacteremia** denotes bacteria in the bloodstream. **Septic shock** is sepsis with hypoperfusion and hypotension refractory to fluid therapy. **Sepsis** refers to a serious infection, localized or bacteremic, that is accompanied by systemic manifestations of inflammation. Sepsis due to bacteremia is often called **septicemia;** this often imprecisely used term is now being discouraged. The more general term, **systemic inflammatory response syndrome,** recognizes that several severe conditions (eg, infections, pancreatitis, burns, trauma) can trigger an acute **inflammatory** reaction, the systemic manifestations of which are associated with release into the bloodstream of a large number of endogenous mediators of inflammation.

Understanding inflammatory mechanisms and discovering better therapies

Inflammatory disease is a major focus for PharmaLinks research. Our research efforts are directed towards target identification, drug discovery, drug assessment in experimental models, development of disease models, pathophysiological investigations, and clinical pharmacology.

Research on inflammation within PharmaLinks benefits from our interdisciplinary collaborations that encompass work at the genetic, molecular and cellular levels, functional *in vitro* and *in vivo* studies and access to disease models. In addition, PharmaLinks draws on the activities of Celsus, a group established in 1993, to foster collaborative research specifically in the field of inflammation between members of the Universities and the Glasgow Royal Infirmary NHS Trust. These links provide a well-established infrastructure that supports clinical trials of anti-**inflammatory** drugs. The clinical units within the Royal Infirmary include the Centre for Rheumatic Diseases and the Respiratory Unit.



The above micrograph (SEM) shows a T-lymphocyte migrating in a collagen network.

Understanding the mechanisms of inflammatory diseases

PharmaLinks has over 100 scientists working in multidisciplinary research teams with tremendous expertise in inflammation and supported by leading edge technologies and facilities. Coupled with direct access to world-renowned clinical trials units, this unique

pool of expertise can be outsourced by our clients for as much of their R&D as required - from drug and target discovery, through drug delivery, to clinical trials. Our core areas of expertise include the following diseases:

Autoimmune diseases

A wide variety of **inflammatory** conditions are linked to autoimmune dysfunction. PharmaLinks has expertise and specialist experimental techniques that have been developed for research in rheumatoid arthritis, systemic lupus erythematosus (SLE), Sjögren's syndrome and ankylosing spondylitis.

New therapy studies that are currently underway include:

- regulation of immune cell response by cytokines and B-cell apoptosis
- cytokine gene therapy
- monoclonal antibody therapy
- interference with antigen recognition

Through PharmaLinks, our clients can also access the Centre for Rheumatic Diseases, which offers considerable expertise in the clinical evaluation of immunotherapeutic agents and new drugs for **inflammatory** joint disease. The Centre has been involved in several important clinical trials in the last ten years including gold, hydroxychloroquine and corticosteroids.

Respiratory disease

Experimental studies in this area are conducted both *in vitro* and *in vivo*, with particular attention being directed towards:

- inflammation and airway remodelling
- influence of humoral factors on airway function
- role of nitric oxide and iNOS in asthma and chronic obstructive pulmonary disease (COPD)
- T-cell regulatory cytokines in asthma and chronic cough
- phosphodiesterases in asthma and COPD clinical therapeutics in asthma, COPD and chronic cough
- extrinsic allergic alveolitis (EAA)
- **neutrophil** elastase (NE) in emphysema, bronchitis, cystic fibrosis, adult and neonatal respiratory distress

PharmaLinks offers a comprehensive range of specialised tests for research in these areas, including respiratory function tests, non-invasive assessment of airway inflammation, invasive assessment of lung pathology and clinical assessment. In addition, PharmaLinks' clients benefit from our access to a large pool of adult and childhood asthmatic volunteers and patients with COPD, chronic cough and other respiratory diseases.

Neuroinflammatory pain

PharmaLinks' scientists and clinical researchers offer expertise in investigating the role of neuropeptides in synovial inflammation, mechanisms affecting proprioceptive responses in **inflammatory** joint disease, and the role of kinin peptides and other **inflammatory** mediators in the production of pain.

This expertise is supported by a large range of *in vitro* and *in vivo* experimental

techniques that are applied to the study of neuroinflammatory pain.

Inflammation after stroke

PharmaLinks has developed models of focal cerebral ischaemia for the study of ischaemic and reperfusion injury associated with experimental stroke. Our current projects include research in the following:

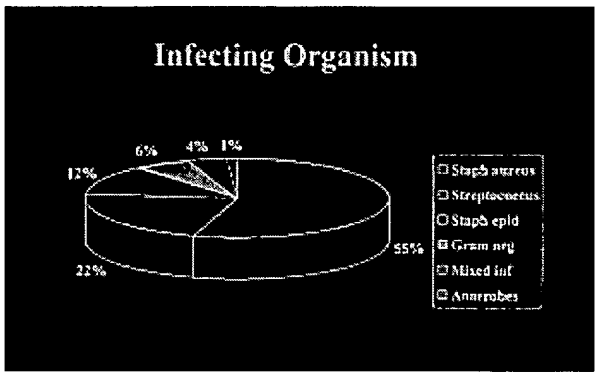
- investigation of the **inflammatory** component of stroke
- potential role of activated microglia in the injury process
- neuroprotective efficacy of a range of anti-oxidant drugs
- role of stroke sensitivity genes
- kynurenine pathway as a drug target for neuroprotective drugs

PharmaLinks also has a particular interest and expertise in mitochondrial and **inflammatory** muscle disease and in studying the immunohistochemistry and molecular biology of muscle in various **inflammatory** and metabolic muscle diseases. PharmaLinks has developed proprietary expertise in this area which is available to clients.

Septic arthritis

Inflammation has long been associated with infection. **Septic** arthritis is a life-threatening complication of rheumatoid arthritis and is also a cause of major morbidity following joint replacement surgery. PharmaLinks has ready access to a clinical database of over 100 patients with **septic** arthritis. Polymorphism studies within this population are currently underway, enabling the identification of individuals at risk from joint infection.

Experimental studies are conducted both *in vitro* and *in vivo*. Animal models, including iNOS deficient mice and NOS2 deficient mice, are being used to investigate the role of **inflammatory** mediators and to test potential therapeutic agents.



A wide variety of infectious agents can cause septic arthritis in humans. The chart shows data from a recent study by Dr M Gupta and Dr M Field at the Centre for Rheumatic Diseases.

Target identification and validation

The control of **inflammatory** mediators is vital in the immune system as they may have both beneficial and detrimental effects. Groups within PharmaLinks are studying the effects of **inflammatory** mediators in a variety of tissues that are likely to be targets for novel anti-**inflammatory** drugs.

Cytokines and inflammation

Research within PharmaLinks includes investigations of the regulation of cytokine production; cell responses to cytokines; the relevance of cytokines (including macrophage and T cell derived cytokines) in **inflammatory** diseases including psoriatic arthritis, **septic** arthritis, rheumatoid arthritis, and SLE; and localisation of immune reactions in the periodontium during disease, in particular the analysis of cytokine production by different cell types.

The role of cytokines in the control of prostaglandin biosynthesis in monocytes and the mechanisms by which prostaglandins and their fatty acid precursors modulate immune cell responses is also a strong area of interest.

Signal transduction in inflammation

The signal transduction mechanisms involved in cellular regulation of biological processes such as apoptosis, proliferation, differentiation and activation are being studied by several groups within PharmaLinks.

The groups aim to identify the molecular basis of a number of **inflammatory** diseases and conditions including asthma, rheumatoid arthritis, and **septic shock**. This will facilitate the development of strategies for intervention in immune dysfunction at the level of drug or gene therapy.

Currently, the pharmaceutical industry is expressing a great deal of interest in:

- mechanisms by which immunomodulatory receptors elicit differentiation
- proliferation and apoptosis in lymphoid and myeloid cells
- the role of G-proteins and protein tyrosine kinases in the regulation of cAMP
- phosphodiesterase inhibitors in the lung
- the regulation of cAMP in the lung
- specific phospholipases and protein kinase (PKC and MAPK) pathways
- the role of PDE4 and 5 isoforms in **inflammatory** diseases

PharmaLinks has research activities in all of these areas and active projects investigating new targets for anti-proliferative and anti-**inflammatory** drugs.

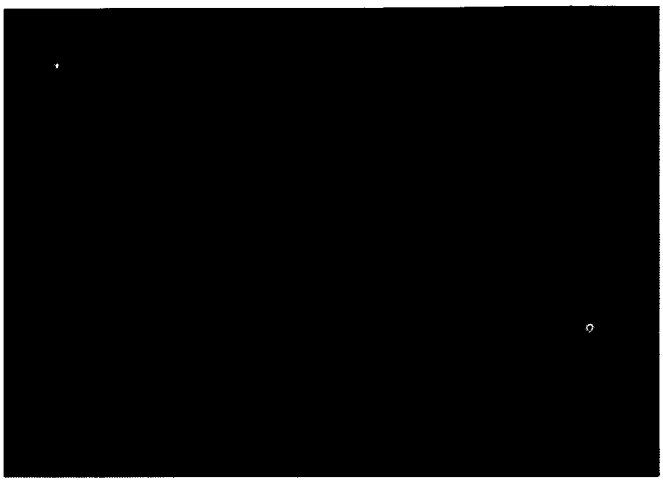
Oxidative stress

Oxidative stress occurs when the body's antioxidant defence mechanisms are unable to cope with the levels of oxidants present and leads to tissue damage. It has been shown to be a factor in a number of **inflammatory** diseases. Within PharmaLinks, several groups are working on projects relating to oxidative stress, with research covering a broad area from physiology through cell biology to chemistry and biochemistry, including:

- development of improved methods of analysis for lipid oxidation products as markers of **inflammatory** processes
- investigation of the molecular events in oxidative damage to lipids by specific oxidants, both in cell membranes and in human low density lipids (LDL)
- use of electrospray mass spectrometry to analyse phospholipid oxidation products and compare their formation with oxidative protein damage
- the contribution of phagocytic cells to oxidative damage

Inflammatory mediators on myocardial function

Part of the work of the cardiovascular research group at PharmaLinks is concerned with the effects of **inflammatory** mediators on myocardial function and on the vasculature.



Interleukin-15 is a pro-inflammatory cytokine implicated in the pathogenesis of a number of human autoimmune diseases. The above fluorescent micrograph demonstrates the presence of IL-15 (green) within human macrophages (nucleus blue) 30 minutes after activation.

Drug discovery and development capabilities

Research relating to drugs and therapeutic compounds within PharmaLinks spans a number of disciplines from chemistry and biomedical sciences to clinical trials.

Anti-**inflammatory** targets

PharmaLinks is investigating several **inflammatory** mediators that are likely to be targets for anti-**inflammatory** drugs and new compounds, including:

- thymosin b-4 sulphoxide
- chemokines, including macrophage **inflammatory** protein 1a (MIP-1a)
- PAR-2
- nuclear factor kappa B (NFkB)
- tumour necrosis factor-alpha (TNFa)

These compounds are being studied using both *in vivo* animal models (e.g. MIP-1a null mouse) and *in vitro* techniques.

Drug discovery screening

The Strathclyde Institute for Drug Research (SIDR), using high throughput screening methods, is screening its extremely diverse natural product library to discover compounds with potential anti-**inflammatory** activity that will lead to the development of new drugs. Current targets include bradykinin receptors, cell adhesion molecules and cytokine pathways.

PharmaLinks has developed experimental models for the evaluation of anti-colitic drugs and has several experimental animal models for the evaluation of anti-**inflammatory** drugs.

Clinical studies

The Centre for Rheumatic Diseases (CRD) has considerable expertise in the evaluation of immunotherapeutic agents such as antibody to TNFa, T cell antibodies and receptor-fusion proteins in the treatment of **inflammatory** joint disease. The CRD is involved in the assessment of biologic agents in the treatment of rheumatoid arthritis, the evaluation of second line drugs in rheumatoid arthritis, and the establishment of a very large database of patients treated with agents such as gold, penicillamine, sulphasalazine and methotrexate. Studies into the mode of action of gold and penicillamine at the molecular level in **inflammatory** joint disease are being carried out by chemists in collaboration with the CRD.

Further information

Our world-class expertise and research facilities are available to companies for contract and collaborative research. Contact PharmaLinks for more information or to discuss how our resources can help increase the speed and expand the scope of your research.

ANSWER 23 OF 23 REGISTRY COPYRIGHT 2001 ACS
RN 458-37-7 REGISTRY
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CN **Curcumin (6CI)**
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CN Curcuma
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CN E 100
CN E 100 (dye)
CN Haidr
CN Halad
CN Haldar
CN Halud
CN Indian Saffron
CN Kacha Haldi
CN Merita Earth
CN Natural Yellow 3
CN **San-Ei Curcumine AL**
CN Souchet
CN Terra Merita
CN **trans,trans-Curcumin**
CN Turmeric
CN Turmeric (dye)
CN Turmeric yellow
CN Ukon
CN Ukon (dye)
CN Yellow Ginger
CN Yellow Root
CN Yo-Kin
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CI COM
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CN 1,6-Heptadiene-3,5-dione, 1-(4-hydroxy-3-methoxyphenyl)-7-(p-hydroxyphenyl)- (8CI)
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OTHER NAMES:
CN **Curcumin II**
CN **Demethoxycurcumin**
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DR 85801-93-0, 91884-87-6, 33171-16-3
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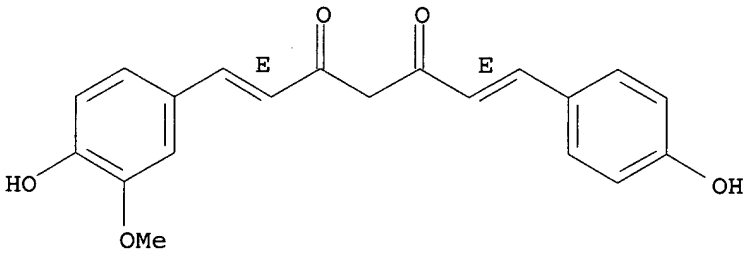

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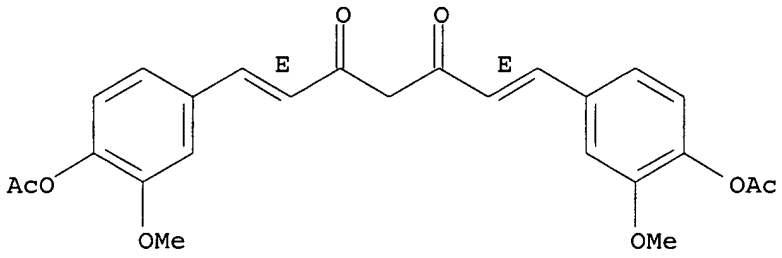

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CN Amanil Fast Yellow AN
CN Atlantic Stilbene Yellow GA
CN Azine Fast Yellow A
CN Azomine Yellow R
CN Bencidal Fast Yellow X
CN Benzanil Yellow R
CN Benzenesulfonic acid, 2-methyl-5-nitro-, alk. cond. products
CN Benzo Fast Yellow A
CN C.I. 40000
CN C.I. Acid Yellow 62
CN Calcomine Yellow 2G
CN Carta Yellow G
CN Carta Yellow G 180
CN Chlorazol Paper Yellow R
CN Chrome Eather Yellow TG
CN Chrome Leather Fast Yellow A
CN Chrome Leather Yellow A
CN Cresotine Yellow A
CN **Curcumine S**
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CN Diazine Yellow R
CN Diazol Fast Yellow A
CN Diphenyl Fast Yellow FA
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CN Direct Fast Yellow AC
CN Direct Fast Yellow R
CN Direct Golden Yellow 2G
CN Direct Orange G
CN Direct Stilbene Yellow
CN Direct Yellow 11
CN Direct Yellow A
CN Direct Yellow F
CN Direct Yellow G
CN Direct Yellow K
CN Direct Yellow MR
CN Direct Yellow Stilbene
CN Direct Yellow T
CN Direct Yellow TG
CN Erie Yellow 2RF
CN Erie Yellow F

CN Erie Yellow FP
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CN Fast Yellow A
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CN Fast Yellow R
CN Fenamin Yellow TP
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CN Fixanol Yellow GS
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MF Unspecified
CI COM, MAN
LC STN Files: CA, CAPLUS, CHEMCATS, CHEMLIST, CIN, CSCHEM, HSDB*, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, PIRA, PROMT, TOXLINE, TOXLIT, USPATFULL
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Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

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48 REFERENCES IN FILE CA (1967 TO DATE)
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48 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L9 ANSWER 7 OF 9 MEDLINE on STN
ACCESSION NUMBER: 95279958 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7760015
TITLE: Human tumor necrosis factor receptor (p55) and interleukin 10 gene transfer in the mouse reduces mortality to lethal endotoxemia and also attenuates local inflammatory responses.
AUTHOR: Rogy M A; Auffenberg T; Espat N J; Philip R; Remick D; Wollenberg G K; Copeland E M 3rd; Moldawer L L
CORPORATE SOURCE: Department of Surgery, University of Florida College of Medicine, Gainesville 32610, USA.
CONTRACT NUMBER: CA-52108 (NCI)
GM-40586 (NIGMS)
SOURCE: Journal of experimental medicine, (1995 Jun 1) 181 (6) 2289-93.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950707
Last Updated on STN: 19950707
Entered Medline: 19950623

AB Anticytokine therapies have been promulgated in gram-negative sepsis as a means of preventing or neutralizing excessive production of proinflammatory cytokines. However, systemic administration of cytokine inhibitors is an inefficient means of targeting excessive production in individual tissue compartments. In the present study, human gene transfer was used to deliver to organs of the reticuloendothelial system antagonists that either inhibit tumor necrosis factor-alpha (**TNF** -alpha) synthesis or block its interactions with cellular receptors. Mice were treated intraperitoneally with cationic liposomes containing 200 micrograms of either a pCMV (cytomegalovirus)/p55 expression plasmid that contains the extracellular domain and transmembrane region of the human p55 **TNF** receptor, or a pcD-SR-alpha/hIL-10 expression plasmid containing the DNA for human interleukin 10. 48 h later, mice were challenged with lipopolysaccharide (LPS) and D-galactosamine. Pretreatment of mice with p55 or IL-10 cDNA-liposome complexes improved survival ($p < 0.01$) to LPS-D-galactosamine. In additional studies, intratracheal administration of IL-10 DNA-liposome complexes 48 h before an intratracheal LPS challenge reduced pulmonary **TNF**-alpha levels by 62% and decreased **neutrophil infiltration** in the lung by 55% as measured by myeloperoxidase activity (both $p < 0.05$). Gene transfer with cytokine inhibitors is a promising option for the treatment of both the systemic and local sequelae of **septic shock**.

ACCESSION NUMBER: 1997:257520 CAPLUS
DOCUMENT NUMBER: 126:233711
TITLE: **Curcumin** (diferuloylmethane) inhibition of NF-.kappa.B activation
INVENTOR(S): Aggarwal, Bharat B.
PATENT ASSIGNEE(S): Research Development Foundation, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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AU 9669773	A1	19970401	AU 1996-69773	19960913
PRIORITY APPLN. INFO.:			US 1995-3799	19950914
			WO 1996-US14725	19960913

AB Because of its intimate involvement in host defense against disease, the NF-.kappa.B transcription factor is an important target for therapeutic intervention. This invention provides a method of inhibiting the activation of the NF-.kappa.B transcription factor in an animal in need of such treatment (e.g. a human with toxic or **septic shock**, radiation damage, graft vs. host reaction, atherosclerosis, AIDS, inflammation or cancer) comprising administering a pharmacol. ED of **curcumin**. Also provided is a method of inhibiting the nuclear translocation of the p65 subunit of the NF-.kappa.B transcription factor in a cell or in an animal in need of such treatment comprising the step of

ACCESSION NUMBER: 95330546 EMBASE
DOCUMENT NUMBER: 1995330546
TITLE: Activation of transcription factor NF-.kappa.B is suppressed by **curcumin** (diferulolylmethane).
AUTHOR: Singh S.; Aggarwal B.B.
CORPORATE SOURCE: Cytokine Research Laboratory, Department of Molecular Oncology, Texas Univ. M. D. Anderson Can. Ctr.,Houston, TX 77030, United States
SOURCE: Journal of Biological Chemistry, (1995) 270/42 (24995-25000).
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB When activated, NF-.kappa.B, a ubiquitous transcription factor, binds DNA as a heterodimeric complex composed of members of the Rel/NF-.kappa.B family of polypeptides. Because of its intimate involvement in host defense against disease, this transcription factor is an important target for therapeutic intervention. In the present report we demonstrate that **curcumin** (diferuloylmethane), a known anti-inflammatory and anticarcinogenic agent, is a potent inhibitor of NF-.kappa.B activation. Treatment of human myeloid ML-1a cells with tumor necrosis factor (TNF) rapidly activated NF-.kappa.B, which consists of p50 and p65 subunits, and this activation was inhibited by **curcumin**. AP-1 binding factors were also found to be down-modulated by **curcumin**, whereas the Sp1 binding factor was unaffected. Besides TNF, **curcumin** also blocked phorbol ester- and hydrogen peroxide-mediated activation of NF-.kappa.B. The TNF-dependent phosphorylation and degradation of I.kappa.B.alpha. was not observed in **curcumin**-treated cells; the translocation of p65 subunit to the nucleus was inhibited at the same time. The mechanism of action of **curcumin** was found to be different from that of protein tyrosine phosphatase inhibitors. Our results indicate that **curcumin** inhibits NF-.kappa.B activation pathway at a step before I.kappa.B.alpha. phosphorylation but after the convergence of various stimuli.

231206 CAPLUS
DOCUMENT NUMBER: 130:232533
TITLE: **Curcumin** (diferuloylmethane) inhibition of NF.kappa.B activation
INVENTOR(S): Aggarwal, Bharat B.
PATENT ASSIGNEE(S): Research Development Foundation, USA
SOURCE: U.S., 15 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5891924	A	19990406	US 1996-712932	19960926

AB A method is provided for inhibiting the activation of the NF.kappa.B transcription factor in an animal in need of such treatment which comprises administering to the animal a pharmacol. ED of **curcumin** . Also provided is a method of inhibiting the nuclear translocation of the p65 subunit of the NF.kappa.B transcription factor in a cell or in an animal in need of such treatment, which comprises administering to the animal a pharmacol. ED of **curcumin**.
REFERENCE COUNT: 3

97:257520 CAPLUS
DOCUMENT NUMBER: 126:233711
TITLE: **Curcumin** (diferuloylmethane) inhibition of NF-.kappa.B activation
INVENTOR(S): Aggarwal, Bharat B.
PATENT ASSIGNEE(S): Research Development Foundation, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9709877	A1	19970320	WO 1996-US14725	19960913
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9669773	A1	19970401	AU 1996-69773	19960913
PRIORITY APPLN. INFO.:			US 1995-3799	19950914
			WO 1996-US14725	19960913

AB Because of its intimate involvement in host defense against disease, the NF-.kappa.B transcription factor is an important target for therapeutic intervention. This invention provides a method of inhibiting the activation of the NF-.kappa.B transcription factor in an animal in need of such treatment (e.g. a human with toxic or **septic** shock, radiation damage, graft vs. host reaction, atherosclerosis, AIDS, inflammation or cancer) comprising administering a pharmacol. ED of **curcumin**. Also provided is a method of inhibiting the nuclear translocation of the p65 subunit of the NF-.kappa.B transcription factor in a cell or in an animal in need of such treatment comprising the step of administering to said animal a pharmacol. ED of **curcumin**.

L7 ANSWER 4 OF 4 EMBASE COPYRIGHT 2001 EL

ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95330546 EMBASE
DOCUMENT NUMBER: 1995330546
TITLE: Activation of transcription factor NF-.kappa.B is suppressed by **curcumin** (diferulolylmethane).
AUTHOR: Singh S.; Aggarwal B.B.
CORPORATE SOURCE: Cytokine Research Laboratory, Department of Molecular Oncology, Texas Univ. M. D. Anderson Can. Ctr.,Houston, TX 77030, United States
SOURCE: Journal of Biological Chemistry, (1995) 270/42 (24995-25000).
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB When activated, NF-.kappa.B, a ubiquitous transcription factor, binds DNA as a heterodimeric complex composed of members of the Rel/NF-.kappa.B family of polypeptides. Because of its intimate involvement in host defense against disease, this transcription factor is an important target for therapeutic intervention. In the present report we demonstrate that **curcumin** (diferuloylmethane), a known anti-inflammatory and anticarcinogenic agent, is a potent inhibitor of NF-.kappa.B activation. Treatment of human myeloid ML-1a cells with tumor necrosis factor (TNF) rapidly activated NF-.kappa.B, which consists of p50 and p65 subunits, and this activation was inhibited by **curcumin**. AP-1 binding factors were also found to be down-modulated by **curcumin**, whereas the Sp1 binding factor was unaffected. Besides TNF, **curcumin** also blocked phorbol ester- and hydrogen peroxide-mediated activation of NF-.kappa.B. The TNF-dependent phosphorylation and degradation of I.kappa.B.alpha. was not observed in **curcumin**-treated cells; the translocation of p65 subunit to the nucleus was inhibited at the same time. The mechanism of action of **curcumin** was found to be different from that of protein tyrosine phosphatase inhibitors. Our results indicate that **curcumin** inhibits NF-.kappa.B activation pathway at a step before I.kappa.B.alpha. phosphorylation but after the convergence of various stimuli.